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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,582	05/24/2006	Steffen Helmling	021315-08220400	6124
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MDIP LLC POST OFFICE BOX 2630 MONTGOMERY VILLAGE, MD 20886-2630			EXAMINER VIVLEMORE, TRACY ANN	
			ART UNIT	PAPER NUMBER
			1635	
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			05/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/522,582	Applicant(s) HEMLING ET AL.	
	Examiner Tracy Vivlemore	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2009 and 05 February 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6,9-14,16-18,20-22,24-27,29-41 and 45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,27 and 45 is/are allowed.
- 6) ☒ Claim(s) 16-18,20-22,24,25 and 29 is/are rejected.
- 7) ☒ Claim(s) 2-4,6,9-14,26 and 30-41 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 November 2008 and 05 February 2009 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/5/08 & 1/30/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Sequence rules compliance

The replies filed 11/5/08 and 2/5/09 have overcome the objections to the drawings regarding compliance with sequence rules.

Allowable Subject Matter

SEQ ID NO: 8 is free of the prior art searched.

Claims 1, 27 and 45 are allowed.

Claim Objections

Claims 2, 6, 12, 13 and 31-36 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Specifically, claim 2 recites that the nucleic acid of claim 1 (SEQ ID NO: 8) is an antagonist of the GHSR 1a receptor system, while claim 6 recites that SEQ ID NO: 8

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specifically binds L-ghrelin, but neither of these claims recite any limitations that provide a structural difference between the sequence of claim 1 and that of claims 2 and 6.

Claims 12, 13 and 31-36 are duplicates of claim 1 for a similar reason. Although these claims recite Kd values for the nucleic acid of claim 1 under different salt conditions, these Kd values do not add structural limitations to the claimed sequence. Because claim 1 recites a particular sequence, the claimed Kd values are assumed in the absence of evidence to the contrary to be a physical characteristic inherent to this sequence.

Claims 3, 4, 9-11, 26 and 30 are objected to because they depend from a duplicate claim, but it is noted that they do further define SEQ ID NO: 8 and would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 14 and 37-41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Each of these claims depends ultimately from claim 6 and recites that the nucleic acid of claim 6 has a variety of lengths ranging from 15-150 to 30-50. However, claim 6 has been limited to SEQ ID NO: 8, which comprises 47 nucleotides, therefore the claims reciting lengths shorter than 47 nucleotides broaden rather than limit the independent claim.

Election/Restrictions

Claims 1, 27 and 45 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 16-18, 20-22, 24, 25 and 29, directed

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to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on January 24, 2007 is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-18, 20-22 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is directed to a method of *in vitro* selection that is used to make the nucleic acid of claim 6. In view of the limitation of claim 6 to SEQ ID NO: 8, this claim is

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indefinite because it does not contain a limitation specifying how performing these selection steps results in production of SEQ ID NO: 8. Claims 17 and 18 are indefinite for the same reason due to their dependence from claim 16.

Claim 20 recites the limitation "the L-nucleic acid of claim 6" in line. There is insufficient antecedent basis for this limitation in the claim because claim 6 is not limited to L-nucleic acids. Claims 21 and 22 are indefinite for the same reason due to their dependence from claim 20.

Claim 29 is directed to a method for screening for a ghrelin antagonist comprising the steps of providing a candidate antagonist and the claimed nucleic acid (SEQ ID NO: 8), providing a test system that provides a signal in the presence of a ghrelin antagonist, and determining whether the candidate compound is a ghrelin antagonist. The metes and bounds of the claim cannot be determined because the relationship of the four elements of the claim is not clearly set forth. Step c recites a test system that provides a signal in the presence of a ghrelin antagonist, however, such antagonists are always present because SEQ ID NO: 8 is claimed as a ghrelin antagonist. Therefore even when the candidate is not a ghrelin antagonist, the system will provide a signal. Additionally, while steps a and b require both a candidate antagonist and a known antagonist, indicating that step d may embrace an assay of competitive binding, the purpose of the known antagonist of step b is not specified. In view of the lack of specified relationship between the known antagonist of step b and what assays are embraced by step d, the purpose of the known antagonist is not known.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

The claims are directed to methods of treating disorders such as obesity, tumors, and cardiovascular disease by administering SEQ ID NO: 8 to a subject. It is noted that claim 24 is actually directed to treatment of a disorder "comprising" ghrelin. This phrase has been interpreted as a method of treating disorders caused by ghrelin.

The specification teaches in the context of a discussion of the prior art that ghrelin directly stimulates the release of growth hormone from the pituitary gland and ghrelin administration in rats resulted in weight gain as a consequence of changes in

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energy intake and/or fuel utilization. The specification further teaches that ghrelin is expressed in a number of neuroendocrine tumors and that injections of ghrelin into healthy individuals increased cardiac output and decreased blood pressure.

In the working examples, the specification discloses (see examples 11 and 12) that an anti-ghrelin speigelmmer inhibited the effects of exogenous ghrelin on growth hormone release and appetite stimulation in rodents. However, in experiments without exogenous ghrelin administration (see examples 8-10) the effects of anti-ghrelin speigelmers were not significantly different from control animals.

No working examples are directed to treatment of any disease. The specification contemplates that ghrelin antagonists can be used to treat other conditions but provides no specific description of such treatment; the discussion of the prior art indicates that a correlation exists between ghrelin expression and pancreatic and tumor cells and cardiovascular activity, but neither the specification nor the prior art teach that this relationship is more than a correlation and do not teach that inhibiting ghrelin actually has any therapeutic effect on these conditions.

While the prior art provides some indication that ghrelin is involved in appetite control, ghrelin has not been used to treat any disease and the reference of Sun et al. (Molecular and Cellular Biology 2003), published shortly after the time of filing, provides evidence that antagonism of ghrelin will not provide a treatment for obesity. Sun et al. teach that while pharmacological studies show that ghrelin stimulates growth hormone release, appetite, and fat deposition, its role in energy homeostasis has not been established. Sun et al. produce ghrelin-null mice that, in contrast to predictions made

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from the pharmacology of ghrelin, are characterized by size, food intake and body composition indistinguishable from wild-type littermates. Sun et al. teach that ghrelin is not likely to be a direct regulator of leptin and insulin and conclude that antagonists of ghrelin are unlikely to have broad utility as antiobesity agents.

In view of the modest effect on food intake observed in the working examples, in order to perform the claimed method of treating obesity, the skilled artisan would have to engage in undue trial and error experimentation to determine what ghrelin antagonists might have a therapeutic effect on obesity. Because the specification and the prior art fail to show a nexus between inhibition of ghrelin activity and treatment of any disease, the skilled artisan would have to perform undue, trial and error experimentation to determine what diseases and conditions could be treated using the claimed nucleic acid sequence. Therefore the claims are not enabled.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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